Smoking and Atherosclerosis. The Letter to the Editor by Burch and Rowell (Br Med J, 23 April, 1966) would be pertinent to examine, relevant to the association between atherosclerosis and smoking.

Smoking and Atherosclerosis

SIR,—You discuss in your leader (26 March, p. 755) the positive association between cigarette smoking and cardiovascular disease. We shall suggest that this is a particular example of a widespread phenomenon.

The sex- and age-distributions[1] of various categories of cardiovascular disease (International Abridged List, 1955: A85, B22–B25, B26—arteriosclerotic and degenerative heart disease—B27, B28, and B29) are all consistent with the view[1,2] that these several diseases have a disturbed-tolerance autoimmune aetiology. This interpretation is supported by the obliterative vascular changes that are observed in kidney homotransplants and which have been attributed to a host-versus-graft reaction.[3] According to the autoimmune theory the cardiovascular disease process is initiated by a small number (generally less than 10) of somatic gene mutations in lymphoid stem cells.[4-6] These spontaneous gene changes initiate the growth of one or more forbidden-clones[4,7] of cells that synthesize autoantibodies. When the target tissue lies behind a blood-tissue barrier the primary autoantibodies are necessarily humoral, and it appears[4,8] that they generally migrate on electrophoresis with the α_2-globulin serum protein fraction. When the target tissue is normally freely infiltrated by small lymphocytes these cells carrying cell-bound autoantibodies act as the primary pathogenic agents. Given this approach, disturbances in the β- and γ-globulin fractions do not represent the primary cause of spontaneous (as opposed to experimental) autoimmune disease but the body's complex response to it.[4,5,8]

Between the initiation of a forbidden-clone and the first manifestation of symptoms or signs a latent period inevitably intervenes. When the primary autoantibodies are cell-bound (lymphocytic), then on the average this interval, for a given environment, is about twice as long in females as in males; but when the target tissue lies behind a blood-tissue barrier the average latent period is usually of about equal duration in the two sexes.[4,5,9] From the clinical evidence we deduce[4,5,9] that the length of the latent period is determined in part by the operation of an intrinsic defence mechanism, which in the case of lymphocytic autoimmunity at least is mediated through immunoglobulins. Forbidden-clones are "foreign" and autoantigenic, and they elicit a classical immune response that restrains their proliferation. Probably all disturbed-tolerance autoimmune diseases can be precipitated and exacerbated by extrinsic factors such as certain infective agents and certain drugs.[5,8] Mental stress produces similar effects.[5,9] We have proposed that these several factors either compete for or affect the level of the defence against forbidden-clones.[5,6] Smoking probably acts in the same way. Anticenic and not-self materials entering the body have to be opsonized and phagocytized, and they therefore compete for the finite defence resources. Consequently, the efficiency of the defence against autoantigenic forbidden-clones is diminished. Autoantibodies increase in number, and the latent or chronic autoimmune condition is precipitated or exacerbated.

The idea that the intrinsic defence mechanism in autoimmunity is vulnerable to various extrinsic factors also accounts for the urban-rural differences that are found in connexion with many chronic conditions: the greater pollution of the urban atmosphere and the greater stress of urban life encourage the growth of forbidden-clones. In our view the effect of cigarette-smoking on cardiovascular disease processes is more appropriately described as exacerbating rather than causal.—We are, etc.,

P. R. J. BURCH.
N. R. ROWELL.

University of Leeds,
General Infirmary,
Leeds 1.

REFERENCES

1. Burch, P. R. J., *Lancet*, 1963, 2, 299.
2. —— *Amer. Heart J.*, 1965, 67, 319.
3. Porter, K. A., Thomson, W. H., Owen, K., Knowles, J. R., Mowbray, J. F., and Peart, W. S., *Brit. med. J.*, 1965, 2, 439.
4. Burch, P. R. J., and Rowell, N. R., *Quart. Rev. Biol.*, 1965, 40, 252.
5. —— and Rowell, N. R., *Acta dermato-venereol. Stockh.*, 1965, 45, 168.
6. Burnet, F. M., *The Clonal Selection Theory of Acquired Immunity*, 1959. London.
7. —— *Brit. med. J.*, 1965, 1, 318.
8. Burch, P. R. J., and Rowell, N. R., *Amer. J. Med.*, 1965, 38, 793.

10050635

Source: https://www.industrydocuments.ucsf.edu/docs/jtlk0000